REMARKS

Claims 48, 51 and 55 are pending. Applicant files herewith a Request for Continued examination and thereby requests entry of these remarks and reconsideration of Applicant's claims in view of the following remarks.

Rejection under 35 U.S.C. § 103(a)

Claims 48, 51 and 55 are rejected as unpatentable over Herron (US Patent 4,764,521) in view of Rubenstein (IDS, CJ) and Rephaeli et al. (US Patent 5,939,455). Applicant traverses.

First, Applicant again reiterates their disagreement with the assertion that Rephaeli teaches 4-PBA or cinnamic acid for treatment of cystic fibrosis. This assertion is premised on a combination of two broadbrush stroke interpretations of two passages: (1) col. 1, lines 15-29 (stating that broad classes of compounds, i.e., oxyalkylene-containing compounds, butyric acid, butyric acid salts, and butyric acid derivatives) are useful for treating any of 14 broad classes of diseases (e.g., cancer, cutaneous ulcers, gastrointestinal disorders, blood disorders, immunomodulation, etc.); and (2) col. 10, lines 18-22, listing 11 compounds as butyric acid derivatives. Applicant disagrees with an assertion that Rephaeli provides a teaching of which compounds are useful against which disease indications with a reasonable expectation of success. Moreover, Rubenstein fails to teach unsaturated, 4-carbon chain compounds, and (as stated in the Action) Herron does not teach unsubstituted aryl carboxylic acid compounds. As such, Applicant traverses as a matter of course that a *prima case* of obviousness is established in the Action.

In the Advisory Action, it is asserted that the claims are not commensurate in scope with the alleged unexpected results. It is further alleged that in the Advisory Action "there is no evidence on the record {that} shows that the mechanism disclosed by Zeitlin is the only biological pathway for treatment of cystic fibrosis. Applicant

provides no explanation as to why cinnamic acid, a compound known to be useful for treatment of cystic fibrosis, is negative in this in vitro method." Applicant disagrees.

In previously submitted declarations, the instantly claimed compound, trans-SAA, is directly demonstrated (as stated in the declaration filed March 5, 2007 in the instant application) to have at least superior activity and/or the presence of an unexpected property over art compounds 4-PBA and cinnamic acid in regard to promotion of trafficking of functional ΔF508-CFTR to the cell surface (which as discussed in detail below, is highly relevant to therapeutic treatment of CF). This is a direct comparison of the claimed subject compound to two art compounds, thus Applicant submits that the scope of the comparison is commensurate. Moreover, Applicant disagrees that Applicant bears any burden for explanation as to why cinnamic acid is negative in the recited *in vivo* method. Applicant has, in her declaration, demonstrated that trans-SAA has the recited superior activity relative to cinnamic acid. That result speaks for itself and is sufficient for the purposes of showing superior activity.

The results establish that trans-SAA is a superior compound relative to 4-PBA or cinnamic acid for promotion of trafficking of functional ΔF508-CFTR to the cell surface. It is further established that restoration of trafficking of the ΔF508-CFTR to the cell membrane results in increased chloride channel function and amelioration of the symptoms of cystic fibrosis (CF) (see Zeitlin, *N. Engl. J. Med.* 351:6 pp. 606-608, previously submitted), and that the mutation involving deletion of a phenylalanine residue at position 508 (ΔF508-CFTR) is a very significant (i.e., 70% of patient population), if not primary, mechanism of CF etiology; thus making control of such trafficking a relevant treatment protocol for a majority of CF patients. As such, the promotion of ΔF508-CFTR trafficking by trans-SAA is a property that is relevant in CF treatment, and Applicants submit that the appropriate nexus between the functional superiority of trans-SAA and treatment of cystic fibrosis is thus established.

Based on the foregoing, Applicant respectfully submits that the rejection is overcome and requests withdrawal of the rejection.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicant's undersigned representative to discuss the application. Applicant thanks the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 49632(71699).

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Respectfully submitted,

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